Message

From: Delinsky, Amy [amy.delinsky@ncdenr.gov]
Sent: 9/29/2020 2:30:45 PM
To: McCord, James [mccord.james@epa.gov]; Strynar, Mark [Strynar.Mark@epa.gov]
Subject: RE: [External] RE: TFA in with early eluters
Attachments: ATT00001.txt

James,

Thank you for the clarification about the amounts of TFA in calibrant and sample—that is helpful to know in discussions with team members about TFA issues.

That is very interesting also that you saw similar ionization charge state issues in grad school work. I think that in this case the idea of pooling/summing responses from the +1/+2 charge state is a good point and may be a good strategy when you can get the +2 charge state response. The later eluting analytes (R-EVE, Nafion Byproduct 4, Nafion Byproduct 5) should have enough mass to see a loss of CO2 from the singly and doubly charged species to do this, and that is something else that can be tested out with existing methods. Of course it will be trickier with the early eluting diprotic analytes.

When we were doing IC/MS/MS analysis at CDC we looked at some lower molecular weight analytes both by pushing the lower mass range of our instrument (well below m/z 100 for some parent and product ions) and by monitoring MRM transitions of [M-H]- to [M-H]- for others. Again, I also do not know if that would be applicable in this situation, but it is an idea. The Sciex instrument specialists told me a while ago that the 5000 (which was supposed to be geared more for smaller molecule work) had a lowest reliable m/z of 50, but we went lower than that using the 4000 at CDC. I am not sure also of the instrument variability in the lower range.

Thank you for the information and conversation about interesting analytical challenges.

Amy

From: McCord, James <mccord.james@epa.gov>
Sent: Tuesday, September 29, 2020 9:30 AM
To: Delinsky, Amy <amy.delinsky@ncdenr.gov>; Strynar, Mark <Strynar.Mark@epa.gov>
Subject: RE: [External] RE: TFA in with early eluters

Amy,

I know the pain of dealing with ion-pairing reagents. We tried some of that in graduate school and ended up having to dedicate an LC system to those solvents because the ion-pair was so intransigent in the pumps.

I believe that you see ion-state differences from the surface water, pH adjusting might have some effect, but the presence of bulk material in surface water (especially like humic acids) can really scavenge excess charge from the ionization and push things into lower charge state. We did some DNA work in grad school and used that strategy to adjust +20/30 molecules down to +5/6 and get better mass accuracy. When we were doing nanospray work we would pool the +1/+2 to avoid issues with charge state interconversion but I don't know how well that works on a low-res MS/MS instrument.

For the chromatogram below that looks to me like overloaded sample TFA combined with the in-source background. Normally we get a sharp peak at the beginning of the gradient and then the background tracks with the organic concentration, but it doesn't saturate to that degree, so there is definitely additional signal from the sample.

--
James McCord

From: Delinsky, Amy [mailto:amy.delinsky@ncdenr.gov]
Sent: Tuesday, September 29, 2020 9:01 AM
To: Strynar, Mark <Strynar.Mark@epa.gov>; McCord, James <mccord.james@epa.gov>
Subject: RE: [External] RE: TFA in with early eluters

They may have been thinking about ion pair chromatography, which can foul up your instrument and HPLC column. I had a method a little over a year ago where I tried really hard to do HILIC to not put ion pair reagent (which is a really different solvent) into the system. The method worked great, and the LC and mass spec were fine after 2 days of flushing with 80:20 IPA:water (the HPLC column has to be dedicated to ion pair methods once the ion pair agent is added to it).

I think ion chromatography would also work well for both the early eluter and diprotic issues because early eluters are retained and monoprotic and diprotic species can be separated. However, not many people have IC systems let alone IC/MS/MS systems (I used one at CDC for perchlorate and other anions), which leaves LC/MS/MS as the most broadly applicable analytical technique for the early eluter and diprotic species.

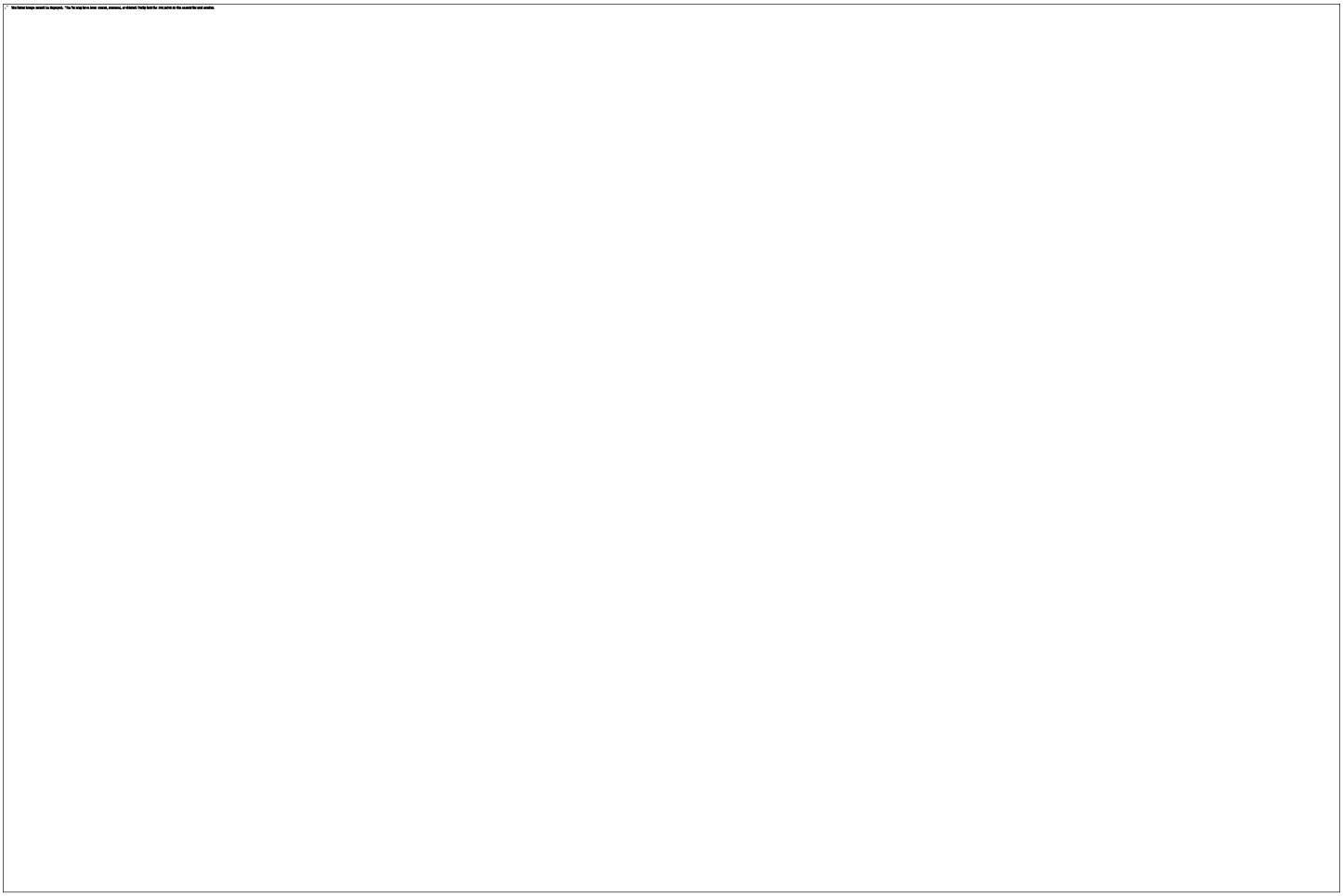
One interesting thing to note is we have some limited evidence that the later eluting diprotic species (R-EVE, Nafion Byproduct 4, Nafion Byproduct 5), method performance is good in spiked lab water (near 100% recovery for all 3 analytes), but bad for spiked surface water samples (500-100% recovery). I am suspecting that there is something in the surface water that changes the ratio of singly and doubly charged analyte in the mass spectrometer. More specifically, I am guessing there is an increase in the amount of singly charged species (the MRM everyone is looking at) in surface water relative to the lab water calibrator leading to an apparent increased concentration in the surface water sample.

The three analytes are not subjected to the same void volume/TFA matrix interferences because they are retained. They coelute, but their performance is okay in lab water which it seems further rules out the analytes suppressing each others ionization, and really seems to leave only something in surface water and something due to ionization in the mass spec due to something in surface water. I have also wondered if pH adjustment of samples would make any difference. Or maybe modifying a lab water sample (which has good recovery) with known additives found in surface water until the sample has high recovery?

So it seems like there are two separate issues – early eluters and diprotic species. The early eluters definitely need different chromatography. There are diprotic early eluters, but also later eluting diprotic analytes which offer a chance to work on those issues with existing methods. Very interesting analytical challenges.

I do have a question for you also—Amy Risen showed me the chromatogram below—I wanted to double check with you—in this chromatogram is the TFA peak due to TFA in the sample or interference from the calibrator? I think it is in the sample, but wanted to check.

Thanks,
Amy



From: Strynar, Mark <Strynar.Mark@epa.gov>
Sent: Monday, September 28, 2020 1:41 PM
To: Delinsky, Amy <amy.delinsky@ncdenr.gov>; McCord, James <mccord.james@epa.gov>
Subject: RE: [External] RE: TFA in with early eluters

Hi Amy good to know. I had people in the pass poopoo on the idea of running HILIC on the same system I use to run our normal LC. I guess I could give it a try. I have a couple of HILIC columns in our arsenal now. I am not sure when I can get to it, but I have a desire and the column needed.

Mark

From: Delinsky, Amy <amy.delinsky@ncdenr.gov>
Sent: Monday, September 28, 2020 11:25 AM
To: Strynar, Mark <Strynar.Mark@epa.gov>; McCord, James <mccord.james@epa.gov>
Subject: RE: [External] RE: TFA in with early eluters

Hi Mark,

Thank you for the information. HILIC actually does not use very different solvents—the difference is essentially that MPA and MPB are switched. Increasing the amount of aqueous in mobile phase (rather than increasing the organic) causes elution of the analytes. I used acetonitrile (MPA) and aqueous ammonium formate (MPB). What is different that may need a different instrument is the following:

Different stationary phase column (I have used an amino column in the past, but there are many different ones now—they are not C18)

Increased re-equilibration time after each run (especially with gradient—often HILIC is actually a mixed retention combined with ion exchange)

Often difficult to run gradients with HILIC

Increased susceptibility to salts in sample with HILIC

Inability to analyze hydrophobic analytes normally run by C18

Yes, with the TFA I also do not know who has added it to their methods, but have heard that it is in samples. I am keeping an eye on it in methods with early eluters because these compounds have issues that may be compounded if they co elute with TFA, and it is very possible for them to co elute with TFA because they should have similar retention mechanisms.

Thanks,
Amy

From: Strynar, Mark <Strynar.Mark@epa.gov>
Sent: Monday, September 28, 2020 11:07 AM
To: Delinsky, Amy <amy.delinsky@ncdenr.gov>; McCord, James <mccord.james@epa.gov>
Subject: [External] RE: TFA in with early eluters

Hi Amy,

I am unsure if Chemours has included TFA. I am also unsure if they used HILIC. What I do know if the Cheours groundwater well samples I have looked at are absolutely loaded with TFA. Beyond the MS suppression it is also one of the calibration masses on our QTOF so we have that issue.

My opinion for the really small, mobile and diprotic PFAS is there needs to be an appropriate method developed to deal with them. HILIC sounds like a good approach, however I think that takes a dedicated piece of equipment as the solvents are very different correct?

Mark

From: Delinsky, Amy <amy.delinsky@ncdenr.gov>
Sent: Monday, September 28, 2020 9:06 AM
To: Strynar, Mark <Strynar.Mark@epa.gov>; McCord, James <mccord.james@epa.gov>
Subject: TFA in with early eluters

Hi Mark and James,

A few other questions related to the early eluters/diprotic compounds. Was TFA included in the mix of compounds analyzed by HILIC? If so, did it elute before, after, or in the middle of the other compounds? I am asking this because TFA by itself is a known ion suppressor in mass spectrometry and so I was wondering if it was resolved from the other early eluter/diprotic compounds.

Also, a long time ago I developed a HILIC method for haloacetic acids (DCA, TCA, and DFA as an internal standard)—this could be a starting point for TFA analysis, and may work for some of the other compounds (or at least give some ideas on how to approach the analytes).

Thanks,

Amy Delinsky, Ph.D.
Environmental Chemist, Division of Waste Management
North Carolina Department of Environmental Quality
919-707-8202
amy.delinsky@ncdenr.gov